



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁴ : A61K 35/78</p>		<p>A1</p>	<p>(11) International Publication Number: WO 88/ 05304</p> <p>(43) International Publication Date: 28 July 1988 (28.07.88)</p>	
<p>(21) International Application Number: PCT/EP88/00034</p> <p>(22) International Filing Date: 20 January 1988 (20.01.88)</p> <p>(31) Priority Application Numbers: 206/87-8 205/87-6 207/87-0</p> <p>(32) Priority Dates: 21 January 1987 (21.01.87) 21 January 1987 (21.01.87) 21 January 1987 (21.01.87)</p> <p>(33) Priority Country: CH</p> <p>(71) Applicant: WILLIAM BLANC & CIE [CH/CH]; 5, place du Molard, CH-1204 Geneva (CH).</p> <p>(72) Inventor: IVONE, Felicia ; Bukit Permai, Blok F I No. 6, Cibubur, Jakarta Timur (ID).</p>			<p>(74) Agents: HRANITZKY, Wilhelm, Max et al.; William Blanc & Cie, 5, place du Molard, CH-1204 Geneva (CH).</p> <p>(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BG, BJ (OAPI patent), BR, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CM (OAPI patent), DE, DE (European patent), DK, FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), HU, IT (European patent), JP, KP; KR, LK, LU, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL, NL (European patent), NO, RO, SD, SE, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	
<p>(54) Title: PROCESSES FOR THE PREPARATION OF MEDICINAL COMPOSITIONS, COMPOSITIONS OBTAINED BY THESE PROCESSES AND USE THEREOF FOR THE PREPARATION OF MEDICINES AGAINST VIRAL HEPATITIS B AND ACQUIRED IMMUNODEFICIENCY SYNDROME</p>				
<p>(57) Abstract</p> <p>Medicines against viral hepatitis B, viral hepatitis "non A, non B" and acquired immunodeficiency syndrome are prepared by extracting simultaneously in boiling water or aqueous medium the following parts of the following plants: <i>Andrographis paniculata</i>: leaves; branches; roots. <i>Cyclea barbata</i>: leaves. <i>Morinda citrifolia</i>: fruits and kernels. <i>Merremia mammosa</i>: tubercules. <i>Curcuma domestica</i>: rhizomes. <i>Curcuma xanthorrhiza</i>: rhizomes. The thus obtained liquid extracts can be administered orally or be used for the preparation of other medical forms. These medicines have a beneficial effect in view of the purification of the blood and elimination of infectious agents within the whole organism.</p>				

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	ML	Mali
AU	Australia	GA	Gabon	MR	Mauritania
BB	Barbados	GB	United Kingdom	MW	Malawi
BE	Belgium	HU	Hungary	NL	Netherlands
BG	Bulgaria	IT	Italy	NO	Norway
BJ	Benin	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	LI	Liechtenstein	SN	Senegal
CH	Switzerland	LK	Sri Lanka	SU	Soviet Union
CM	Cameroon	LU	Luxembourg	TD	Chad
DE	Germany, Federal Republic of	MC	Monaco	TG	Togo
DK	Denmark	MG	Madagascar	US	United States of America
FI	Finland				

PROCESSES FOR THE PREPARATION OF MEDICINAL COMPOSITIONS,
COMPOSITIONS OBTAINED BY THESE PROCESSES AND USE THEREOF
FOR THE PREPARATION OF MEDICINES AGAINST VIRAL
HEPATITIS B AND ACQUIRED IMMUNODEFICIENCY SYNDROME

The present invention relates to a process of preparation of a medicinal composition called "DUANA PAKEN HEPATITIS B" as well as to processes of preparation of medicinal compositions respectively called "SAKARIA AIDS I" and "SAKARIA AIDS II".

The invention further relates to the compositions obtained by these processes and to the use of the composition called "DUANA PAKEN HEPATITIS B" for the preparation of a medicine against hepatitis B virus and hepatitis virus "non A, non B", as well as to the use of the compositions called "SAKARIA AIDS I" and "SAKARIA AIDS II" for the preparation of medicines against acquired immunodeficiency syndrome.

The invention results from the discovery of new therapeutic properties of medicinal compositions obtained by extracting simultaneously in boiling water or aqueous medium specified parts of several plants which grow in South East Asia, and in particular in Indonesia, and which have already been individually used in traditional medicine in that part of the world. It should be noted that therapeutic properties of the composition according to the invention are different from a simple addition of the known healing virtues of each of the plants used in this preparation.

However, prior to a detailed description of the invention, the known properties and therapeutic applications in the area of "traditional" or "natural" medicine of the plants in question, such as they have been described in the literature, will now be indicated:

Andrographis paniculata :

This plant has been used to combat general frailness as well as colic, dysentery, certain forms of dyspepsia and anorexia, cachexy and syphilitic ulcers. Its leaves and roots are considered to possess febrifuge, stomachic and tonic properties.

Cyclea barbata :

This plant contains the alcaloide called "cycleine" which imparts to it a very bitter taste. It has a very high starch content and contains about 10% fat. Its leaves may be used to prepare a jelly which is considered as a medicine against gastric troubles.

Morinda citrifolia :

The leaves of this plant contain an essential oil and its fruits are used in traditional medicine against dysentery and asthma as well as a desobstruent and as an emmenagogue. The juice, obtained by squeezing its leaves, is applied externally. The roots are cathartic and it has been reported that a decoction of the roots has an emetic and laxative effect. The infusions of the leaves are considered as emollients, sedatives and stomachic.

Merremia mammosa (plant with edible tubercles):

The tubercles have been used as a remedy against diabetes, as well as against infections of the throat and the respiratory organs and against tuberculosis of the lung.

Curcuma domestica (Curcuma longa) and Curcuma xanthorrhiza :

These plants contain phenolic compositions, in particular curcumine and flavonoides. They are used as a condiment, a dye and as a medicinal substance (tonic and carminative).

According to a first embodiment of the invention, the process of preparation of a medicinal composition called "DUANA PAKEN HEPATITIS B" comprises the steps of simultaneously subjecting leaves, stalks and/or roots, of the plant "Andrographis paniculata", leaves of the plant "Cyclea barbata", fruits and kernels of the plant "Morinda citrifolia" and roots of the plant "Merremia mammosa" to extraction in aqueous medium.

According to a second embodiment of the invention, the process of preparation of a medicinal composition called "SAKARIA AIDS I" comprises the steps of simultaneously subjecting leaves, stalks and/or roots of the plant "Andrographis paniculata", leaves of the plant "Cyclea barbata", fruits and kernels of the plant "Morinda citrifolia" and roots of the plant "Merremia mammosa" to extraction in aqueous medium so as to obtain a first aqueous extract, and then simultaneously subjecting leaves, stems and/or roots of the plant "Andrographis paniculata" and roots of the plant "Merremia mammosa" to extraction by said first aqueous extract so as to obtain a second aqueous extract which constitutes the final product.

According to a third embodiment of the invention, the process of preparation of a medicinal composition called "SAKARIA AIDS II" comprises the steps of simultaneously subjecting leaves, stalks and/or roots of the plant "Andrographis paniculata", leaves of the plant "Cyclea barbata", fruits and kernels of the plant "Morinda citrifolia" and roots of the plant "Merremia mammosa" to extraction in aqueous medium so as to obtain a first liquid extract, and then simultaneously subjecting rhizomes of the plant "Curcuma domestica" and rhizomes of the plant "Curcuma xanthorrhiza" to extraction in said first liquid extract so as to obtain a second liquid extract which constitutes the final product.

The designations and characteristics of the plants used in

combination for the preparation of the medicinal compositions according to the invention are respectively the following:

A: Andrographis paniculata : (Acanthaceae family)

Taste	bitter
Colour of the leaves	green to dark green
Colour of the branches	dark green to brownish
Colour of the flowers	violet to white

B: Cyclea barbata : (Menispermaceae family)

Taste	bitter and sharp
Colour of the leaves	dark green to light brown (with velvet like fleece)

C: Morinda citrifolia : (Rubiaceae family)

Taste	sharp, bitter and sweet
Colour of the fruits	
- young fruit	green
- older fruit	yellow to light brown (with marks)

D: Merremia mammosa : (Convolvulaceae family)

Designations	merremia mammosa; iponoa memosa; convolvulus mammosa; batatta mammosa
--------------	---

E: Curcuma domestica : (Zingiberaceae family)

Designations	Curcuma longa or Curcuma domestica
--------------	---------------------------------------

Taste	bitter and sharp
Colour of the rhizomes	yellowish to orange

F: Curcuma xanthorrhiza : (Zingiberaceae family)

Taste	bitter
Colour of the rhizomes	yellowish to orange

The gathering conditions and the treatment of the parts of the plants preliminary to the preparation of the composition are preferably the following:

A: Andrographis paniculata :

<u>Parts used</u>	leaves; branches (stalks); roots
-------------------	-------------------------------------

Gathering conditions and preliminary treatment:

The parts used are collected from fresh plants, aged between 6 months and one and a half year. They are washed and then dried in the sun, preferably on glass plates until they are completely dessicated, taking care not to let them turn brownish yellow or black in colour. After drying, the leaves, branches and roots are cut up into pieces of 5 to 8 cm.

B: Cyclea barbata :

<u>Parts used</u>	leaves (only)
-------------------	---------------

Gathering conditions and preliminary treatment:

Leaves of plants aged between one year and a half and two years are collected and washed several times in cold water, taking care not to crush them. After this, each leaf is cut up into three parts. Only fresh leaves are

used.

C: Morinda citrifolia :

Parts used fruits and kernels

Gathering conditions and preliminary treatment:

Fresh fruit which is ripe or almost ripe is gathered from plants between four and six years old. The fruits are washed in warm water until they are clean, then each fruit is cut up into eight to ten pieces and the kernel is taken out.

D: Merremia mammosa :

Parts used roots (tubercules)

Gathering conditions and preliminary treatment:

Tubercules from plants aged two to three years and a half are picked out and washed in warm water several times until they are clean. After that, they are peeled, taking off the skin very thinly, then cut up into slices having preferably a width of 2 to 3 mm. During the peeling of the roots, the gum initially white, turns to brown and will run out.

E: Curcuma domestica :

Parts used rhizomes

Gathering conditions and preliminary treatment:

The rhizomes are taken from plants aged between one year and a half and three years and washed in warm water

several times until they are clean. Thereafter, the rhizomes are peeled, taking out the skin very finely, then cut up into slices of preferably 2 to 3 mm in width. During the peeling step, a yellow gum will flow out of the rhizomes.

F: Curcuma xanthorrhiza :

Parts used rhizomes

Gathering conditions and preliminary treatment:

The rhizomes are taken from plants aged between one and a half year and three years and washed several times in warm water until they are clean. Thereafter, the rhizomes are peeled, taking out the skin very finely, then cut into slices of preferably 1 to 1.5 mm in width. During the peeling step, a gum will flow out of the rhizomes. Said gum which is initially yellowish subsequently turns to brown-yellow in colour.

A detailed description of best modes of carrying out the process according to the invention will now be given by way of examples of particular embodiments.

Example 1:

(Preparation of a "strong" composition of "DUANA PAKEN HEPATITIS B")

In a cooking vessel provided with an airtight lid, a stirring device and a security valve which prevents the pressure inside the recipient from surpassing a value equal to or slightly greater than atmospheric pressure parts of the plants designated above by the letters A, B, C and D, to be extracted in water are placed in four respective layers and the total volume of the water used as an aqueous.

extraction medium is added.

The initial disposition in the cooking vessel and the relative proportions of the parts of the plants to be extracted are the following (for an initial total volume of 8 litres of water by way of aqueous extraction medium):

a) first layer from the bottom:

Plant "D" : 18 kg (corresponding to the weight of the fresh or partially dried roots, before peeling and cutting into slices)

b) second layer from the bottom:

Plant "C" : 12 kg (pieces of fresh fruit)

c) third layer from the bottom:

Plant "B" : 4 kg (parts of fresh leaves)

d) fourth layer from the bottom (top layer):

Plant "A" : 6 kg (pieces of leaves, stems and dried roots)

The extraction is carried out by progressively increasing the temperature of the water from room temperature to boiling point in 5 hours, then maintaining the extraction medium at boiling point for 3 hours, during a second heating phase immediately subsequent to the first one. At the end of this second heating step, the volume of liquid medium is reduced to about 4 or 5 litres from the initial amount of 8 litres.

One finally carries out the third heating phase which consists of maintaining the extraction medium at boiling point for about one hour and a half, while stirring up three or four times in order to mix the different parts of the contents of the cooking vessel.

After separating the solids, a liquid product which is dark

brown in colour or still has a brown tint with yellow, pink, red or green hue is thus obtained. This liquid product constitutes the medicinal composition according to the invention.

Example 2:

(Preparation of a "weak" composition of "DUANA PAKEN HEPATITIS B")

The same procedure as in the preceding case is followed but with the following relative proportions of the parts of the plants to be extracted: (for an initial water volume of 3 to 4,5 litres):

- a) Plant "D" : 4 to 6 kg (weight of the fresh or partially dried roots before they are peeled and cut up in slices)
- b) Plant "C" : 4 kg
- c) Plant "B" : 1,5 to 2 kg
- d) Plant "A" : 1 kg

In this case, the respective durations of the first, second and third phases of the heating process are 5 hours, 2 hours and 1 hour.

The compositions obtained by proceeding as described above ("strong" or "weak" composition) can be stored for several weeks, or even several months, preferably in a cool place and in a water-tight container, without any change except for an increase in its bitterness and astringency.

In order to improve its keeping properties, it may be useful to reheat the composition several times, for example about every 4 days during the first few days following its

preparation.

The liquid extracts obtained in the manner indicated above, can be used either as a pharmaceutical potion to be administered orally to the patient, or for the preparation of other medical forms such as tablets, pellets, capsules or injectable liquid. To this end, one can proceed in an appropriate manner according to the usual preparation techniques for galenical methods and for industrial pharmaceutical products.

For example, for the preparation of injectable liquid from the initial liquid extract, one can distill the latter to recover an anhydrous essence which is used in the preparation of injectable forms of medicines. These allow a more pronounced curative effect than that which results from the oral administration of the initial liquid extract.

The medicinal compositions obtained as described in the above examples 1 and 2 are efficient for the treatment of hepatitis virus "non A, non B". Moreover, they are equally seen to have a curative effect against chronic ulcers and intestinal infections of the lungs and the kidneys, and more generally a beneficial effect in view of the purification of the blood and the elimination of infectious agents, such as the viruses, within the whole organism.

The doses to be given depend on the illness to be treated, as well as on the constitution and general state of health of the patient.

For example, for the treatment of chronic hepatitis B, or hepatitis "non A, non B", one can give orally the "strong" composition (obtained in the manner described above) in doses of 30 to 40 ml, every four hours, likewise after meals, to patients of a weaker constitution or who have a frailer state of health.

It should be noted that the "strong" composition should only be administered to patients who are not suffering from other illnesses such as, for example, diabetes, further to viral B hepatitis.

The "weak" composition can be administered to patients suffering from acute hepatitis B or to those suffering, in addition to hepatitis B, from additional illnesses such as diabetes or other complications relating to their general health.

The dosage for the "weak" composition can be favourably 50 to 60 ml, three times a day, for a non diabetic patient. In the case of a diabetic patient, the dose can be reduced to 30 to 4 ml, twice a day during the first four days, then reduced to 50 to 60 ml twice a day the following days, alternating with the administration of the usual medicine against diabetes.

Secondary effects can be noted. In particular, amongst the number of secondary effects, intestinal contractions may occur 4 to 8 times, after taking the liquid extract, during the first 3 or 4 days, as well as a very pronounced diuretic and sudorific effect, which generally disappears after 3 or 4 days of continuous treatment.

In order to avoid dehydration and feelings of weakness in the body, inherent in the diuretic and sudorific effect, the patient should drink large quantities of sugared water (except, of course, in the case of a diabetic patient, where the "strong" dosage is counter-indicated).

Patients should preferably rest during the duration of the treatment. They can eat normally, avoiding spices, alcohol and products with a high fat content, especially oils. A vegetarian diet is particularly appropriate. Patients should moreover refrain from smoking.

A treatment followed as outlined above permits an improvement in the patient's condition after only 3 to 4 days, with a complete cure in 2 to 4 weeks in cases of moderate acute chronic hepatitis, 3 to 4 weeks in the case of chronic viral hepatitis and 3 to 6 weeks in the case of hepatitis with complications.

Example 3:

(Preparation of a medicinal composition called "SAKARIA AIDS I")

In a cooking vessel provided with an air tight lid, a stirring device and a security valve which prevents the pressure inside the recipient from exceeding an amount equal to or slightly greater than atmospheric pressure, parts of the above specified plants designated by the letters A, B, C and D are put in four distinct overlying layers and the total volume of the water to be used as the first extraction medium is added.

The initial disposition in the vessel and the relative proportions of the parts of the plants destined to be extracted are the following (for an initial volume of 12 litres of water):

a) first layer from the bottom:

Plant "D": 18 to 20 kg (corresponding to the weight of fresh or partially dried roots, before being peeled and cut up into slices)

b) second layer from the bottom:

Plant "A": 7 kg (bits of leaves, stalks and dried roots)

c) third layer from the bottom:

Plant "C": 12 to 14 kg (pieces of fresh fruit)

d) fourth layer from the bottom (top layer):

Plant "B": 4 to 6 kg (parts of fresh leaves).

The extraction is carried out by progressively increasing the temperature of the water from room temperature to boiling point in 5 hours, then maintaining the extraction medium at boiling point for 3 hours, during a second heating step immediately subsequent to the first one. At the end of this second heating step, the volume of the liquid medium is reduced to about 5 or 6 litres.

One carries out finally a third phase of heating in which the extraction medium is maintained at boiling point for two hours, while stirring up twice or three times the contents of the vessel in order to mix the different parts thereof.

After separating the residual solids, a liquid extract of dark brown colour or which has a brown tint verging on green, yellow, pink or red is obtained.

In a cooking vessel identical to that used to carry out the first extraction, parts of the two plants "D" (2 to 4 kg) and "A" (2 to 3 kg) are placed in two distinct overlying layers, in that order starting from the bottom, and 5 or 6 litres of the first liquid extract to be used as the extracting medium for the final extraction are added into the vessel.

A final extraction is then carried out, bringing progressively the extraction medium to boiling point.

The final extraction liquid, which constitutes the desired medicinal composition, is of a colour analogous to that of the first liquid extraction. It has a sharp, sweet and very

bitter taste.

This composition can be kept for several weeks, or even several months, preferably in a cool place and in a water tight container without any change in its composition other than a progressive increase in its bitterness and astringency.

One can use the composition obtained in the manner indicated above, such as a pharmaceutical potion to be administered orally to the patient or for the preparation of other medicinal forms such as tablets, pellets, capsules or injectable liquid. To this end one can proceed in the appropriate manner according to the usual techniques for galenical methods and for industrial pharmaceutical products.

For example, for the preparation of injectable liquid from the liquid extract, one can distill the latter in order to obtain an anhydrous essence which is used in the preparation of injectable forms of medicines. This permits a more pronounced curative effect to be obtained than in the case of oral administration of the liquid extract.

The medicinal composition obtained in the above indicated manner is highly effective in treating AIDS (Acquired Immunodeficiency Syndrome).

The doses to be given depend on the constitution and general state of health of the patient.

In general, the liquid composition obtained in the manner described above, may be given orally in doses of 40 to 50 ml, taken at intervals of three hours. For the treatment of patients with a very bad general health conditions, the doses should preferably be reduced to 30 to 40 ml every three hours.

The medicinal composition obtained as described in the present Example 3 can be given either alone or alternatively with the medicinal composition called "SAKARIA AIDS II", the preparation method of which is described above and in the following Example 4.

Example 4:

(Preparation of a medicinal composition called "SAKARIA AIDS II"):

In a cooking vessel provided with an air tight lid, a stirring device and a security valve which prevents the pressure inside the recipient from exceeding a value equal to or slightly greater than atmospheric pressure, parts of the plants specified above and respectively designated by the letters A, B, C and D are positioned in four successive distinct and overlying layers and the total volume of water used as the extraction medium is added.

The initial disposition in the vessel and the relative proportions of the parts of the plants to be extracted are the following (for an initial total volume of 12 litres of water):

a) first layer from the bottom:

Plant "D": 18 to 20 kg (corresponding in weight to fresh or partially dried roots, before being peeled and cut up in slices).

b) second layer from the bottom:

Plant "A": 7 kg (pieces of leaves, stalks and dried roots)

c) third layer from the bottom:

Plant "C": 12 to 14 kg (pieces of fresh fruit)

d) fourth layer from the bottom (top layer):

Plant "B": 4 to 6 kg (parts of fresh leaves).

The extraction is carried out by raising the temperature of the water progressively from room temperature to boiling point in 5 hours, then maintaining the extraction medium at boiling point for 3 hours during a second heating period which is immediately subsequent to the first one. At the end of this second heating step, the volume of liquid medium is reduced to about 5 or 6 litres.

One carries out finally a third heating phase in which the extraction medium is maintained at boiling point for 2 hours, while stirring up the contents of the vessel so as to mix the different parts thereof.

After separating the residual solid parts, a first liquid extract which is brown in colour or which has a brown tint verging on green, yellow, pink or red hue is obtained.

In a cooking vessel identical to that used to carry out the first extraction, the rhizomes of the two plants "E" (2 to 3 kg) and "F" (3 to 4 kg) are then placed in two distinct overlying layers and 5 to 6 litres of the first liquid extract to be used as the extracting medium for the final extraction are added into the vessel.

A final extraction is then carried out, bringing progressively in three hours the extraction medium to boiling point.

The final liquid extract which constitutes the desired medicinal composition, has a colour analogous to that of the first liquid extraction. Its taste is sharp, sweet and very bitter.

This composition can be kept for several weeks, or even several months, preferably in a cold place and in a water tight container, without any change occurring in its composition other than a progressive increase in its bitterness and its astringency.

One can use the composition obtained as described in Example 4 as a pharmaceutical potion to be administered orally to the patient, or for the preparation of other medicinal forms such as tablets, pellets, capsules or injectable liquid. To this end, one can proceed in the appropriate manner according to the usual galenic preparation techniques and for industrial pharmaceutical products.

For example, for the preparation of injectable liquid from the liquid extract, one can distill the latter in such a way so as to gather an anhydrous essence which is used in the preparation of injectable forms of medicines. This permits a more pronounced curative effect to be obtained than in the case when the liquid extract is taken orally.

The medicinal composition obtained in the above indicated manner is effective in treating AIDS (Acquired Immunodeficiency Syndrome).

The doses to be given depend on the constitution and the general health of the patient.

In general, the liquid composition obtained in the manner described above may be given orally in doses of 40 to 50 ml, taken at 3 hourly intervals. For the treatment of patients who have a very weak general condition, it is preferable to reduce the dose to 30 to 40 ml, to be taken every three hours.

The medicinal composition obtained according to the present Example 4 can be given either alone or alternatively with

the medicinal composition called "SAKARIA AIDS I", the preparation method of which is described above in particular in Example 3.

Secondary effects can also be observed as a result of the administration of the compositions obtained as described in Examples 3 and 4. In particular, amongst the number of secondary effects, one can note intestinal contractions which can occur 4 to 8 times after the consumption of the liquid extract, during the first 3 to 4 days, as well as a very pronounced diuretic and sudorific effect, which generally disappears at the end of 3 or 4 days of continuous treatment.

In order to fortify the patient's organism and to avoid dehydration and the inherent weakening as a result of the diuretic and sudorific effect, the patient should drink large quantities of sugared water.

The patient should preferably rest during the duration of the treatment. He can eat normally, but must avoid spices, alcohol and products with a high fat content, especially oils. A vegetarian diet is particularly appropriate. The patient should moreover refrain from smoking.

A treatment regularly followed, without interruption, according to the conditions mentioned in Examples 3 and 4 above, will permit, in general, a cure after 6 to 8 weeks.

CLAIMS

1. A process of preparation of a medicinal composition called "DUANA PAKEN HEPATITIS B", comprising the step of simultaneously subjecting leaves, stalks and/or roots of the plant "Andrographis paniculata", leaves of the plant "Cyclea barbata", fruits and kernels of the plant "Morinda citrifolia" and roots of the plant "Merremia mammosa" to extraction in aqueous medium.

2. A process according to claim 1, wherein the extraction is carried out by maintaining the parts of the plants immersed in the aqueous medium and progressively raising the temperature of said medium from room temperature to boiling point and then maintaining the temperature of the extraction medium at the boiling point.

3. A process according to claim 2, wherein the length of time for heating the aqueous medium from room temperature to boiling point is of 5 hours and the period of maintaining the extraction medium at the boiling point is of 3 hours.

4. A process according to claims 2 or 3, wherein the relative proportions of the parts of the plants subjected to extraction are the following (for an initial volume of 8 litres of extraction medium):

- Andrographis paniculata (in a dried form) : 6 kg
- Cyclea barbata (in a fresh form) : 4 kg
- Morinda citrifolia (in a fresh form) : 12 kg
- Merremia mammosa (in a fresh or partially dried form) : 18 kg

5. Process according to claims 2 or 3, wherein the relative proportions of the plants subjected to extraction are the following (for an initial volume of 3 to 4,5 litres of extraction medium):

- *Andrographis paniculata* (in a dried form) : 1 kg
- *Cyclea barbata* (in a fresh form) : 1,5 to 2 kg
- *Morinda citrifolia* (in a fresh form) : 4 kg
- *Merremia mammosa* (in a fresh or partially dried form) : 4 to 6 kg

6. Medicinal composition called "DUANA PAKEN HEPATITIS B", obtained by the process according to one of claims 1 to 5.

7. Use of the composition according to claim 6 for the preparation of a medicine against hepatitis virus "non A, non B".

8. A process of preparation of a medicinal composition called "SAKARIA AIDS I", comprising the steps of simultaneously subjecting leaves, stalks and/or roots of the plant "*Andrographis paniculata*", leaves of the plant "*Cyclea barbata*", fruits and kernels of the plant "*Morinda citrifolia*" and roots of the plant "*Merremia mammosa*" to extraction in aqueous medium so as to obtain a first aqueous extract, and then simultaneously subjecting leaves, stems and/or roots of the plant "*Andrographis paniculata*" and roots of the plant "*Merremia mammosa*" to extraction by said first aqueous extract so as to obtain a second aqueous extract which constitutes the final product.

9. A process according to claim 8, wherein the first aqueous extract is prepared by maintaining the parts of the plants to be extracted immersed in the aqueous medium and

progressively raising the temperature of said medium from room temperature to boiling point and then maintaining the extraction medium at boiling point, separating the thus obtained aqueous extract from the residue of the plants subjected to the extraction step, immersing in this first aqueous extract the parts of the plants to be subjected to extraction in this extract and finally progressively increasing the temperature of the whole mixture thus obtained up to the boiling point of the liquid part thereof.

10. A process according to claim 9, wherein during the first extraction step the duration of the heating step until boiling point is reached is of 5 hours and the period of maintaining the liquid at boiling point is of 3 hours, whereby the extraction medium is maintained substantially at rest, and the duration of the subsequent boiling step is of 2 hours, whereby the extraction medium is stirred.

11. A process according to claims 9 or 10, wherein during the first extraction step the length of time for raising the temperature of the aqueous extraction medium at boiling point is of 3 hours.

12. A process according to claim 8, wherein during the first extraction step the relative proportions of the different plants subjected to extraction are the following (for an initial volume of 12 litres of the aqueous extraction medium):

- *Merremia mammosa* (fresh or partially dried) : 18 to 20 kg
- *Andrographis paniculata* (fresh) : 7 kg
- *Morinda citrifolia* (fresh) : 12 to 14 kg
- *Cyclea barbata* (fresh) : 4 to 6 kg

13. A process according to claim 12, wherein during the step of extraction by the first aqueous extract the relative proportions of the two plants extracted are the following (for an initial volume of the first aqueous extract of 5 to 6 litres):

- *Merremia mammosa* (fresh or partially dried) : 2 to 4 kg
- *Andrographis paniculata* (dry) : 2 to 3 kg

14. Medicinal composition "SAKARIA AIDS I" obtained by the process according to claims 8 to 13.

15. Use of the composition according to claim 14 for the preparation of a medicine against acquired immunodeficiency syndrome.

16. A process of preparation of a medicinal composition called "SAKARIA AIDS II", comprising the steps of simultaneously subjecting leaves, stalks and/or roots of the plant "*Andrographis paniculata*", the leaves of the plant "*Cyclea barbata*", fruits and kernels of the plant "*Morinda citrifolia*" and the roots of the plant "*Merremia mammosa*" to extraction in aqueous medium so as to obtain a first liquid extract and then simultaneously subjecting rhizomes of the plant "*Curcuma domestica*" and rhizomes of the plant "*Curcuma xanthorrhiza*" to extraction in said first liquid extract so as to obtain a second liquid which constitutes the final product.

17. A process according to claim 16, wherein the first liquid extract is prepared by maintaining the parts of the plants to be extracted immersed in the aqueous medium and progressively raising the temperature of said medium from room temperature to boiling point and then maintaining the extraction medium at boiling point, separating the liquid extract from the residue of the plants subjected to the extraction step, immersing in the thus obtained liquid

extract the parts of plants to be subjected to extraction in this extract and progressively increasing, finally, the temperature of the whole mixture thus obtained up to the boiling point of the final liquid extraction product.

18. A process according to claim 17, wherein during the first extraction step, the length of time for the heating step until boiling point is reached is 5 hours and the period of maintaining the first extraction medium at boiling point is 3 hours, whereby the extraction medium is maintained substantially at rest, followed by a subsequent boiling step of 2 hours, whereby the extraction medium is subjected to stirring action.

19. A process according to claims 17 or 18, wherein, during the first extraction step, the length of time for raising the temperature of the aqueous extraction medium to the boiling point is of 3 hours.

20. A process according to claim 16, wherein during the first extraction step the relative proportions of the plants subjected to extraction are the following (for an initial volume of 12 litres of the aqueous extraction medium):

- *Merremia mammosa* (fresh or partially dried): 18 to 20 kg
- *Andrographis paniculata* (dried) : 7 kg
- *Morinda citrifolia* (fresh) : 12 to 14 kg
- *Cyclea barbata* (fresh) : 4 to 6 kg

21. A process according to claim 16, wherein during the step of extraction by the first liquid extract the relative proportions of the parts of the two plants to be extracted are the following (for an initial volume of the first liquid extract of 5 to 6 litres):

24

- Curcuma domestica : 2 to 3 kg
- Curcuma xanthorrhiza : 3 to 4 kg

22. Medicinal composition called "SAKARIA AIDS II" obtained by the process according to claims 16 to 21.

23. Use of the composition according to claim 22 for the preparation of a medicine against acquired immunodeficiency syndrome.

INTERNATIONAL SEARCH REPORT

International Application No **PCT/EP 88/00034**

I. CLASSIFICATION F SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC ⁴ : A 61 K 35/78								
II. FIELDS SEARCHED <div style="text-align: right; font-size: small;">Minimum Documentation Searched ⁷</div> <table style="width: 100%; border: none;"> <tr> <td style="width: 25%; border: none;">Classification System</td> <td style="border: none;">Classification Symbols</td> </tr> <tr> <td style="border: none; vertical-align: top;">IPC⁴</td> <td style="border: none; vertical-align: top;">A 61 K</td> </tr> </table> <div style="text-align: center; font-size: x-small; margin-top: 10px;"> Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸ </div>			Classification System	Classification Symbols	IPC ⁴	A 61 K		
Classification System	Classification Symbols							
IPC ⁴	A 61 K							
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹ <table border="1" style="width: 100%; border-collapse: collapse; font-size: x-small;"> <tr> <th style="width: 10%;">Category ⁹</th> <th style="width: 60%;">Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²</th> <th style="width: 30%;">Relevant to Claim No. ¹³</th> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 10px;">A</td> <td style="padding: 10px;"> Commonwealth Agriculture Bureau, CAB, ref. no. 77764229, R.R. Kaleysa: "Screening of indigenous plants for anthelmintic action against human Ascaris lumbricoides. Part II", see the abstract & Indian Journal of Physiology and Pharmacology, vol. 19, no. 1, 1975, p. 47-49 <div style="text-align: center; margin-top: 20px;">-----</div> </td> <td style="text-align: center; vertical-align: top; padding: 10px;">1</td> </tr> </table>			Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	A	Commonwealth Agriculture Bureau, CAB, ref. no. 77764229, R.R. Kaleysa: "Screening of indigenous plants for anthelmintic action against human Ascaris lumbricoides. Part II", see the abstract & Indian Journal of Physiology and Pharmacology, vol. 19, no. 1, 1975, p. 47-49 <div style="text-align: center; margin-top: 20px;">-----</div>	1
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³						
A	Commonwealth Agriculture Bureau, CAB, ref. no. 77764229, R.R. Kaleysa: "Screening of indigenous plants for anthelmintic action against human Ascaris lumbricoides. Part II", see the abstract & Indian Journal of Physiology and Pharmacology, vol. 19, no. 1, 1975, p. 47-49 <div style="text-align: center; margin-top: 20px;">-----</div>	1						
<div style="display: flex; justify-content: space-between; font-size: x-small;"> <div style="width: 45%;"> <p>[*] Special categories of cited documents: ¹⁰</p> <p>^{"A"} document defining the general state of the art which is not considered to be of particular relevance</p> <p>^{"E"} earlier document but published on or after the international filing date</p> <p>^{"L"} document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>^{"O"} document referring to an oral disclosure, use, exhibition or other means</p> <p>^{"P"} document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>^{"T"} later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>^{"X"} document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>^{"Y"} document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>^{"A"} document member of the same patent family</p> </div> </div>								
IV. CERTIFICATION <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> Date of the Actual Completion of the International Search <div style="text-align: center; font-size: large;">22nd April 1988</div> </td> <td style="width: 50%; border: none; vertical-align: top;"> Date of Mailing of this International Search Report <div style="text-align: center; font-size: large;">25.05.88</div> </td> </tr> <tr> <td style="border: none; vertical-align: top;"> International Searching Authority <div style="text-align: center; font-weight: bold;">EUROPEAN PATENT OFFICE</div> </td> <td style="border: none; vertical-align: top;"> Signature of Authorized Officer <div style="text-align: center;"> P.-E.G. VAN DER PUTTEN </div> </td> </tr> </table>			Date of the Actual Completion of the International Search <div style="text-align: center; font-size: large;">22nd April 1988</div>	Date of Mailing of this International Search Report <div style="text-align: center; font-size: large;">25.05.88</div>	International Searching Authority <div style="text-align: center; font-weight: bold;">EUROPEAN PATENT OFFICE</div>	Signature of Authorized Officer <div style="text-align: center;"> P.-E.G. VAN DER PUTTEN </div>		
Date of the Actual Completion of the International Search <div style="text-align: center; font-size: large;">22nd April 1988</div>	Date of Mailing of this International Search Report <div style="text-align: center; font-size: large;">25.05.88</div>							
International Searching Authority <div style="text-align: center; font-weight: bold;">EUROPEAN PATENT OFFICE</div>	Signature of Authorized Officer <div style="text-align: center;"> P.-E.G. VAN DER PUTTEN </div>							